

CLAIMS

1. (Withdrawn) An isolated nucleic acid sequence, of an alternative splicing variant, selected from the group consisting of:

(i) the nucleic acid sequence depicted in any one of SEQ ID NO: 1 to SEQ ID NO: 26;

(ii) nucleic acid sequences having at least 90% identity with the sequence of (i) with the proviso that each sequence is different than the original nucleic acid sequence from which the sequences of (i) have been varied by alternative splicing; and

(iii) fragments of (i) or (ii) of at least 20 b.p., provided that said fragment contains a sequence which is not present, as a continuous stretch of nucleotides, in the original nucleic acid sequence from which the sequences of (i) have been varied by alternative splicing.

2. (Withdrawn) An isolated nucleic acid sequence according to Claim 1, having at least 95% identity to any one of SEQ ID NO: 1 to SEQ ID NO: 26.

3. (Withdrawn) An isolated nucleic acid sequence complementary to the nucleic acid sequence of Claim 1.

4. (Previously Amended) An amino acid sequence selected from the group consisting of:

(i) an amino acid sequence coded by an isolated nucleic acid sequence of alternative splice variants selected from the group consisting of:

(a) the nucleic acid sequence depicted in any one of SEQ ID NO: 1 to SEQ ID NO: 26;

(b) nucleic acid sequences having at least 90% identity with the sequence of (a) with the proviso that each sequence is different than the original nucleic acid sequence from which the sequences of (a) have been varied by alternative splicing; and

(c) fragments of (a) or (b) of at least 20 b.p., provided that said fragment contains a sequence which is not present, as a continuous stretch of nucleotides, in the original nucleic acid sequence from which the sequences of (a) have been varied by alternative splicing; and

(ii) homologues of the amino acid sequences of (i) in which one or more amino acids has been added, deleted, replaced or chemically modified in the region or adjacent to the region where the amino acid sequences differs from the original amino acid sequence, coded by the original nucleic acid sequence from which the variant has been varied.

5. (Previously Amended) An amino acid sequence according to Claim 4, as depicted in any one of SEQ ID NO: 27 to SEQ ID NO: 52.

6. (Withdrawn) An isolated nucleic acid sequence coding for any one of the amino acid sequences of Claim 5.

7. (Withdrawn) A purified antibody which binds specifically to any of the amino acid sequence of Claim 4.

8. (Withdrawn) An expression vector comprising any one of the nucleic acid sequences of Claim 1 and control elements for the expression of the nucleic acid sequence in a suitable host.

9. (Withdrawn) An expression vector comprising any one of the nucleic acid sequences of Claim 3, and control elements for the expression of the nucleic acid sequences in a suitable host.

10. (Withdrawn) A host cell transfected by the expression vector of Claim 8.

11. (Withdrawn) A host cell transfected by the expression vector of Claim 9.

12. (Previously Amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and as an active ingredient an agent selected from the group consisting of:

(i) an expression vector comprising

(A) an isolated nucleic acid sequence of alternative splice variants selected from the group consisting of:

(a) the nucleic acid sequence depicted in any one of SEQ ID NO: 1 to SEQ ID NO: 26;

(b) nucleic acid sequences having at least 90% identity with the sequence of (a) with the proviso that each sequence is different than the original nucleic acid sequence from which the sequences of (a) have been varied by alternative splicing; and

(c) fragments of (a) or (b) of at least 20 b.p., provided that said fragment contains a sequence which is not present, as a continuous stretch of nucleotides, in the original nucleic acid sequence from which the sequences of (a) have been varied by alternative splicing; and

(B) control elements for the expression of the nucleic acid sequence in a suitable host; and

(ii) any one of the amino acid sequences of Claim 4.

13. (Original) A pharmaceutical composition according to Claim 12, for treatment of diseases which can be ameliorated or cured by raising the level of any one of the amino acid sequences depicted in SEQ ID NO: 27 to SEQ ID NO: 52.

14. (Original) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and as an active ingredient an agent selected from the group consisting of:

- (i) any one of the nucleic acid sequences of Claim 3;
- (ii) the expression vector of Claim 9; and
- (iii) the purified antibody of Claim 7.

15. (Original) A pharmaceutical composition according to Claim 14, for treatment of diseases which can be ameliorated or cured by decreasing the level of any one of the amino acid sequences depicted in SEQ ID NO: 27 to SEQ ID NO: 52.

16. (Original) A method for detecting an variant nucleic acid sequence in a biological sample, comprising the steps of:

- (a) hybridizing to nucleic acid material of said biological sample any one of the nucleic acid sequences of Claim 1; and
- (b) detecting said hybridization complex;

wherein the presence of said hybridization complex correlates with the presence of an variant nucleic acid sequence in the said biological sample.

17. (Original) A method for detecting an variant nucleic acid sequence in a biological sample, comprising the steps of:

- (a) hybridizing to nucleic acid material of said biological sample any one of the nucleic acid sequences of Claim 3; and
- (b) detecting said hybridization complex;

wherein the presence of said hybridization complex correlates with the presence of an variant nucleic acid sequence in the said biological sample.

18. (Original) A method for determining the level of variant nucleic acid sequences in a biological sample comprising the steps of:

- (a) hybridizing to nucleic acid material of said biological sample any one of the nucleic acid sequences of Claim 1; and
- (b) determining the amount of hybridization complexes and normalizing said amount to provide the level of the variant nucleic acid sequences in the sample.

19. (Original) A method for determining the level of variant nucleic acid sequences in a biological sample comprising the steps of:

(a) hybridizing to nucleic acid material of said biological sample any one of the nucleic acid sequences of Claim 3; and

(b) determining the amount of hybridization complexes and normalizing said amount to provide the level of the variant nucleic acid sequences in the sample.

20. (Original) A method for determining the ratio between the level of variant of the nucleic acid sequence in a first biological sample and the level of the original sequence from which the variant has been varied by alternative splicing in a second biological sample comprising:

(a) determining the level of the variant nucleic acid sequence in the first biological sample according to the method of Claim 19;

(b) determining the level of the original sequence in the second biological sample; and

(c) comprising the levels obtained in (a) and (b) to give said ratio.

21. (Original) A method according to Claim 20, wherein said first and said second biological samples are the same sample.

22. (Original) A method according to Claim 20, wherein the nucleic acid material of said biological sample are mRNA transcripts.

23. (Original) A method according to Claim 22, where the nucleic acid sequence is present in a nucleic acid chip.

24. (Original) A method for identifying candidate compounds capable of binding to the variant product and modulating its activity the method comprising:

(i) providing any one of the amino acid sequences as defined in Claim 4;

(ii) contacting a candidate compound with said amino acid sequence;

(iii) determining the effect of said candidate compound on the biological activity of said protein or polypeptide and selecting those compounds which show a significant effect on said biological activity.

25. (Original) A method according to Claim 24, wherein the compound is an activator and the measured effect is increase in the biological activity.



26. (Original) A method according to Claim 24, wherein the compound is an deactivator and the effect is decrease in the biological activity.

27. (Original) An activator of any one of the amino acid sequences of Claim 4.

28. (Original) An deactivator of any one of the amino acid sequences of Claim 4.

29. (Original) A method for detecting any one of the amino acid sequences of Claim 4 in a biological sample, comprising the steps of:

(a) contacting with said biological sample the antibody of Claim 7, thereby forming an antibody-antigen complex; and

(b) detecting said antibody-antigen complex

wherein the presence of said antibody-antigen complex correlates with the presence of the desired amino acid in said biological sample.

30. (Original) A method for detecting the level of any one of the amino acid sequence of Claim 4 in a biological sample, comprising the steps of:

(a) contacting with said biological sample the antibody of Claim 7, thereby forming an antibody-antigen complex; and

(b) detecting the amount of said antibody-antigen complex and normalizing said amount to provide the level of said amino acid sequence in the sample.

31. (Original) A method for determining the ratio between the level of any one of the amino acid sequences of Claim 4 present in a first biological sample and the level of the original amino acid sequences from which they were varied by alternative splicing, present in a second biological sample, the method comprising:

(a) determining the level of the amino acid sequences of Claim 4 into a first sample by the method of Claim 30;

(b) determining the level of the original amino acid sequence in the second sample; and

(c) comparing the level obtained in (a) and (b) to give said ratio.

32. (Original) A method according to Claim 31, wherein said first and said second biological samples are the same sample.

33. (Original) A method for detecting any one of the antibodies of Claim 7 in a biological sample comprising the steps of:

(a) contacting said biological sample with any one of the amino acid sequences of Claim 4 thereby forming an antibody-antigen complex; and

(b) detecting said antibody-antigen complex

wherein the presence of said antibody-antigen complex correlates with the presence of the antibody in said biological sample.

34. (Original) A method for detecting the level of any one of the antibodies of Claim 7 in a biological sample comprising the steps of:

(a) contacting said biological sample with any one of the amino acid sequences of Claim 4;

(b) detecting the amount of said antibody-antigen complex and normalizing said amount to provide the levels of said antibody in the sample.

35. (New) An amino acid sequence according to claim 4, wherein said amino acid sequence consists of SEQ ID NO: 42 and is coded by an isolated nucleic acid sequence which consists of SEQ ID NO: 16.

36. (New) A pharmaceutical composition comprising:

a pharmaceutically acceptable carrier and as an active ingredient an expression vector comprising an isolated nucleic acid sequence consisting of SEQ ID NO: 16 and control elements for the expression of the nucleic acid sequence in a suitable host; and

the amino acid sequence of Claim 35.